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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/074,472	05/07/1998	MARK M. RICHTER	09481.0027	2284

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/074,472	RICHTER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *30-33* is/are allowed.

6)☒ Claim(s) *34-46 and 50-59* is/are rejected.

7)☒ Claim(s) *47-49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 3, 2007 has been entered.

Status

2. Claims 30-59 are pending.

Claims 34-46 and 50-59 are rejected.

Claims 30-33 are allowed.

Claims 47-49 are objected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 34-35, 38-40, 42-46 and 50-59 are rejected under 35 U.S.C. 102(e) as being anticipated by Bohannon (U.S. Patent 5,763,158).

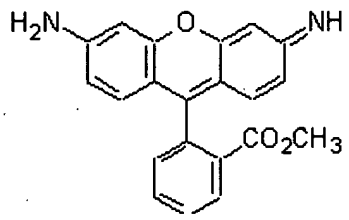
Bohannon teaches a method for detecting an "analyte" in a sample composition (see column 3, lines 18-32) comprising the steps of:

(a) preparing an assay mixture comprising:

(i) said sample composition (see column 4, lines 5-35, where the sample is a "ligand" in the terminology of Bohannon),

(ii) a first reagent comprising an ECL label having a chemical moiety that has electrochemical properties, which ECL label is capable of providing an observed ECL emission (see column 4, lines 10-60 and particularly column 4, line 58 where the ECL label ruthenium (II) tris(bipyridyl) chelate is used),

(iii) a second reagent having an ECL quenching moiety that, when in quenching contact with an ECL label, attenuates the observed ECL emission thereby providing a reduced ECL emission, said ECL quenching moiety comprising at least one benzene moiety (see column 4, lines 25-30 "The mAB is labeled with a quencher molecule capable of reducing detectable reporter activity and see lines 35-46, particularly line 42, where Rhodamine is identified as a quencher whose structure is shown below and comprises a "benzene" moiety)



(b) bringing the assay mixture into contact with a working electrode (see column 4, lines 15-21),

(c) applying a potential to the electrode, thereby enabling an electrochemiluminescence reaction to proceed (see column 4, lines 15-21, "applying a low voltage to an electrode position near the binding site"),

(d) detecting a difference between the observed ECL emission and the reduced ECL emission, thereby confirming the presence of said analyte in the sample solution (see column 4, lines 30-35 and claim 1, step (b)).

With regard to claims 35, 38 and 39, Bohannon teaches benzene carboxylic moieties (see column 4, line 42, where Rhodamine is used and Rhodamine comprises a "benzene carboxylic" moiety).

With regard to claims 40, 42, Bohannon teaches an ECL reagent with ruthenium (II) tris(bipyridyl) chelate (see column 4, line 58).

With regard to claims 43-44, Bohannon teaches attachment of the ECL label and bringing the quencher into quenching contact by interactions of the analyte and binding partner (seee column 4, lines 15-35).

With regard to claims 45-46, 50-57, 59, Bohannon teaches the use of antigens and antibodies as ligands (see column 3, lines 17-32).

With regard to claim 58, Bohannon teaches the ligand may be antibodies and the detector can be antibodies (see column 3, lines 17-32).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 36, 37 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohannon (U.S. Patent 5,763,158) in view of Kuzmin et al (J. Photochem. Photobiol. A: Chem (1995) 87:43-54).

Bohannon teaches the limitations of claims 34-35, 38-40 and 42 as discussed above. Bohannon teaches the use of any quencher that will quench the ruthenium molecule, expressly claiming "the quencher compound absorbs light at 620 nm" (see claim 26, for example).

Bohannon does not expressly teach the quenchers of quinones, phenols or the use of Osmium as the ECL reagent.

Kuzmin teaches a method for detecting an "analyte" in a sample composition (see page 44, column 2, where SDS micelles and the different micelle concentrations are the analytes) comprising the steps of:

(a) preparing an assay mixture comprising:

(i) said sample composition (see page 44, column 2, where SDS micelles and the different micelle concentrations are the analytes),

(ii) a first reagent comprising an ECL label having a chemical moiety that has electrochemical properties, which ECL label is capable of providing an observed ECL emission (see figure 1 and abstract, where Ruthenium bipyridine is used),

(iii) a second reagent having an ECL quenching moiety that, when in quenching contact with an ECL label, attenuates the observed ECL emission thereby providing a reduced ECL emission, said ECL quenching moiety comprising at least one benzene moiety (see table 1, where several different quinones were used)

(b) detecting a difference between the observed ECL emission and the reduced ECL emission, thereby confirming the presence of said analyte in the sample solution (see figure 3, where SDS micelles resulted in differential quenching).

With regard to claims 35-37, Kuzmin teaches quinone moieties which encompass phenols (see table 1).

With regard to claims 40, 42, Kuzmin teaches an ECL reagent with Ruthenium bipyridine (see abstract, table 1).

Kuzman teaches that Ruthenium and Osmium are known prior art equivalents, but does not exemplify the assay with Osmium (see page 51, column 2, paragraph 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the phenolic or quinone quenchers of Kuzmin into the method of Bohannon since Bohannon expressly desired quenchers which quench Ruthenium bipyridine and Kusmin teaches compounds which quench Ruthenium bipyridine (see abstract). Further, it would have been prima facie obvious to use osmium for ruthenium since Kuzmin teaches that these are known equivalents. As MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process

for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

Allowable Subject Matter

8. Claims 30-33 are allowed.

9. Claims 47-49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. The following is a statement of reasons for the indication of allowable subject matter: Claims 30-33 and claims 43-59 are drawn to inventions in which the analytes are nucleic acids used in hybridization and for claims 30-33, where the quenching molecule is limited to phenol or benzoquinone and oligonucleotide interactions are required. While Bohannon clearly teaches application of an ECL method with a quencher in a protein based system, Bohannon does not suggest nucleic acid detection methods. The newly cited DiCesare reference suggests nucleic acid detection methods using ECL, but does not suggest the use of a quencher. There is insufficient motivation between the two references to properly combine these references to make a case of prima facie obviousness. In the absence of such motivation, no proper case of prima facie obviousness exists and the claims are novel and unobvious over the prior art.

Response to Arguments

11. Applicant's arguments filed January 3, 2007 have been fully considered but they are not persuasive.

Applicant first repeats the argument that Bohannan does not teach rhodamine as an ECL quencher. In order to anticipate, Bohannon is simply required to teach the elements of the claim. As noted previously, Bohannan teaches that rhodamine can function as a quencher in the same column as the discussion of the ECL reaction. Bohannan is open to any quencher which will function at 620 nM.

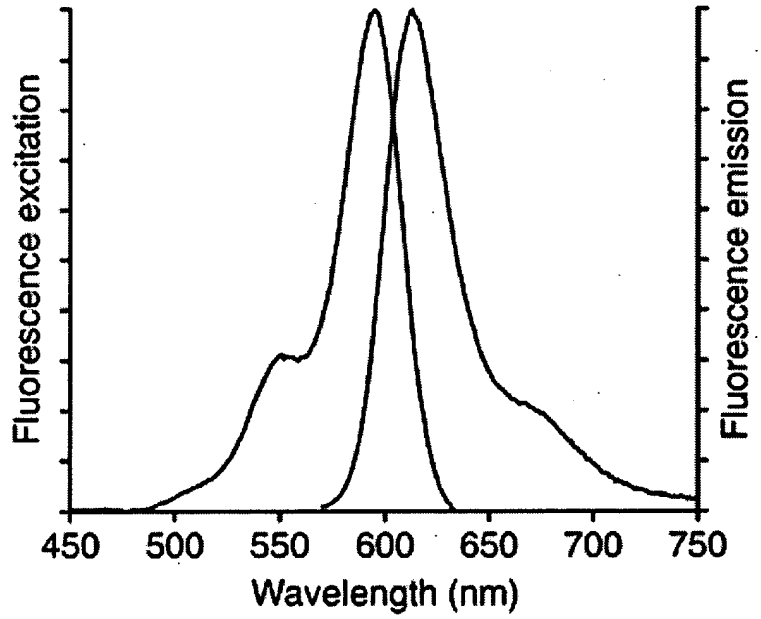
Essentially, Applicant uses the next several pages to attempt to limit the disclosure of Bohannan from the broad, any quencher which will function at 620 nM, and the teaching that rhodamine is such a quencher, when Bohannan is applied as an anticipatory, 102 rejection. There is no requirement in a 102 rejection that the reference teach the elements in a single place in a single embodiment. Whether Bohannan appreciated that rhodamine would also function in the FRET assay does not distinguish when there is a broad teaching in Bohannan that any molecule which would quench at 620 nM would function in the assay.

Applicant then argues that rhodmine might not function as an ECL label. With respect to this argument, the teaching of Bohannan is a positive statement that rhodamine can quench. There is no evidence that it would not function as an ECL label. As MPEP 716.01(c) notes,

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Here, the statements regarding any inoperability of the prior art must be demonstrated, not simply argued.

Further, as noted previously, , the emission spectrum of Sulforhodamine 101 Sulfonyl Chloride is shown below, and this spectrum clearly encompasses 620 nm for absorbance.



This demonstrates that this rhodamine molecule, at least, would be expected to absorb at the wavelength desired by Bohannan.

Applicant then argues the 103 rejection by arguing that the compounds of Kuzmin might not function as quenchers as required by Bohannan. This is much too limiting a read of obviousness. Bohannan wishes quenchers and believes that they must quench a 620 nM. However, Bohannan wishes to quench ruthenium (II)

tris(bipyridyl) chelate (see column 4, line 58), which is the precisely same compound being investigated by Kuzmin. An ordinary practitioner would certainly appreciate that compounds which quench in the assay of Kuzmin would be expected to quench in the assay of Bohannan. As MPEP 2112.01 notes "Products of identical chemical composition can not have mutually exclusive properties." Here, an ordinary practitioner would be motivated to use quenchers taught as function for ruthenium (II) tris(bipyridyl) chelate by Kuzmin in the assay of Bohannan.

With regard to the equivalency issue, Kuzmin expressly shows the use of Ruthenium and Osmium as equivalents. Applicant has argued that the environment is different but provides no data in the specific assay to demonstrate that this equivalency is wrong. That is, given the teaching by Bohannan to use ECL labels such as ruthenium (see column 4, line 13) and given the teaching by Kuzmin that ruthenium and osmium are known in the prior art as equivalents (see teachings of Kuzmin discussed above), in the absence of any secondary consideration, substitution of equivalents is prima facie obvious.

Conclusion

12. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued

examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

3/1/04